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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,956	07/14/2001	Avi Ashkenazi	10466/66	4189

30313 7590 01/13/2005

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,956	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-46 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 27, 2004 has been entered.

Response to Amendment

2. Claims 42-46 have been amended and claims 39- 41 and 47 have been cancelled as requested in the amendment filed on October 27, 2004. Claims 42-46 and 49-51 are pending in the instant application.

Claims 42-46 and 49-51 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on October 27, 2004 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Objections

6. Claims 42-43 are objected to because of the following informalities: claims 42-43 depend from cancelled claim 39. Appropriate correction is required.

Claim Rejections - 35 USC § 101

7. Claims 42-46 and 49-51 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for those reasons of record in section 7 of Paper No. 10 and in section 5 of Paper mailed on April 27, 2004. Briefly, the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

Applicant traverses the rejection on the premises that Examples 74 and 77 are "not a toxicity test but ha[ve] routinely been used to identify several well-known proinflammatory molecules like blood coagulation factor XIII, VEGF, etc" (bottom at page 5 of the Response), that "PRO 266 is an inflammatory molecule useful in treating inflammatory conditions like autoimmune diseases" (top at page 6) and refers to Declaration of Sherman Fong, Ph.D.

Applicant's arguments and the Declaration of Fong under 37 CFR 1.132 filed on October 04, 2004 have been fully considered but are insufficient to overcome the rejection of claims 42-46 and 49-51 based upon 35 U.S.C. 101 as set forth in the last Office action for the reasons that follow.

At section 7 of the Declaration, Dr. Fong presents a view of a role of proinflammatory molecules with respect to vascular permeability and explains possible events that occur at the site

of injury or infection. At section 8, it is further stated that "proinflammatory molecules are useful in treating infections" because of their ability to stimulate immune cells; that some proinflammatory molecules may cause tissue destruction; and that proinflammatory molecules can be useful in reducing tumor growth because of their ability to inhibit neovascularization. Sections 9-12 describe the Skin Vascular Permeability Assay and its use in studies applying different factors, including growth factors.

There appears to be no disagreement on the role of proinflammatory molecules as presented in the Declaration of Fong and the view existing in the art. For example, it is well described in the art that proinflammatory proteins ("molecules") are known to play a key role in the migration of inflammatory cells in autoimmune diseases and in invasive cancers (see Opdenakker et al, 2002, Verh. K. Acad. Geneeskd Belg., 64 (2), pp. 105-36, page 123, Summary). It is also recognized in the art that the spectrum of action of proinflammatory molecules is very broad and also dependent on the timing and level of production of a specific proinflammatory protein. Falcone et al. publication (Falcone et al., 1999, Curr. Opin. Immunol., 11 (6), pp. 670-6) discloses, for example, that TNF, a proinflammatory cytokine, can have anti-inflammatory and protective effects against T-cell mediated autoimmunity (page 671, first column); or that "IL-12 is another proinflammatory cytokine, critical for inducing Th1 differentiation, that has also downmodulated inflammatory autoimmune responses" (page 671, second column). It is concluded in review article by Falcone et al. that "cytokines may have completely contradictory roles according to the time they enter the scene in the process of T-cell-mediated autoimmunity. In addition, cytokines may play an unexpected role in autoimmunity by modulating cellular populations other than T cells" (page 672, first column). Thus, the art

acknowledges the broad range and complexity of functions of proinflammatory proteins and, therefore, the specific function of a particular molecule cannot be predicted based solely on the notion that it belongs to a family of proinflammatory proteins.

At section 13 of the Declaration, Dr. Fong repeats the description of the experiments as disclosed in Examples 74 and 77 on pages 208-210 of the instant specification and further states "that the PRO polypeptide that shows activity in the Skin Vascular permeability assay has specific, substantial and credible utilities. [...] Examples of utilities include, enhancing immune cell recruitment to sites of injury or infection, or inhibitors to treat autoimmune diseases such as psoriasis" (section 14 of the Declaration).

In view of art recognition of broad range of functions of proinflammatory molecules, the disclosure that the instant PRO 266 molecules displayed proinflammatory features in Skin Vascular Permeability Assay does not render the asserted utility specific, since the specification does not establish that PRO266 proteins are specifically associated with a particular immune condition, such as autoimmune disease, for example, including psoriasis. It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. In the instant case, significant further research would have to be conducted to identify diseases, which could be treated by administration of PRO 266 proteins. Therefore, this asserted utility is also not substantial.

To grant Applicant a patent encompassing an isolated naturally occurring human protein, which is not readily usable in it's current form, would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole

areas of scientific development, without compensating benefit to the public" *Brenner v. Manson*, *Ibid*). To grant Applicant a patent on the claimed PRO266 polypeptide based solely upon an assertion that this protein belongs to a family of proinflammatory molecules is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

The Examiner maintains that because the instant specification does not disclose a credible "real world" use for the claimed polypeptides, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

8. Claims 42-46 and 49-51 stand rejected under 35 U.S.C. 112, first paragraph for reasons of record in section 8 of Paper No. 10 and in section 6 of Paper mailed on April 27, 2004. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Claims 42-43, as amended, stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record in section 9 of Paper No. 10 and in section 7 of Paper mailed on April 27, 2004.

Applicant submits that "the specification provides detailed description about the cloning and expression of variants of the polypeptide PRO2666 [...], and describes an assay for testing

the ability of PRO266 polypeptide, including variants of the native sequence, to induce a proinflammatory response. Thus, Applicants indicate that the genus of proteins that are variants of PRO266 must also possess the ability to induce a proinflammatory response and must have at least 95% identity to the sequence of SEQ ID NO: 91" (top at page 7 of the Response). Applicant's arguments have been carefully considered but are not persuasive for the following reasons.

As fully explained in the previous communications of record, to satisfy written description requirement under 35 U.S.C. 112, first paragraph, a specification must describe the entire genus of the claimed polypeptides, which are, in the instant case, proteins with 95% and 99% sequence identity to the amino acid sequence having SEQ ID NO: 91, which "induce an inflammatory response". However, contrary to Applicant's statement, the instant specification fails to disclose the complete structure of the claimed polypeptides, or to identify a particular portion of the structure that must be conserved to retain the claimed function. It is also not clear how many members are in the claimed genus of proteins, those polypeptides that have 95% or 99% of sequence identity to a polypeptide of SEQ ID NO: 91 and have any relevance to the instant PRO266 protein. Thus, it can be concluded that the claims are directed to subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 42-46 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 42-44, as amended, are vague and ambiguous in section (c), which now recites "; or the amino acid sequence" etc. Appropriate correction is required.

12. Claims 45-46 and 49-51 are indefinite for being dependent from indefinite claims.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

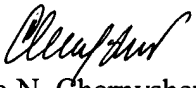
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

January 10, 2005